REMARKS

Reconsideration of the allowability of the present application is requested respectfully.

Status of the Claims

Claims 1 to 5 and 15 to 20 were acted upon by the Examiner in the Office Action dated May 5, 2003. No claims are withdrawn. Claims 1 and 15 have been amended. No claims have been cancelled. Claims 35 to 46 have been added. Accordingly, Claims 1 to 5, 15 to 20, and 35 to 46 are presented for examination.

Support for the amendments to Claims 1 and 15 is found throughout the application, particularly from page 5, line 13, to page 6, line 2.

Support for Claims 35 to 46 can be found throughout the application, particularly on page 5, lines 13 to 21; page 15, lines 5 to 9; page 16, lines 19 to 20; Table 1 on page 16; Table 2 on page 17; and in originally filed Claims 1 to 5 and 15 to 20.

ARGUMENTS

In response to the Examiner's Office Action dated May 2, 2003, Applicant respectfully traverses the Examiner's rejection of Claims 1 to 6 and 15 to 20.

The §112, First Paragraph, Rejections of Claims 1 to 6 and 15 to 20

The Examiner has rejected Claims 1 to 6 and 15 to 20 under 35 U.S.C. §112 as containing new subject matter. In particular, the Examiner asserts that the specification does not support microparticles that are "at least 0.6 μm". In response to this assertion, applicant has amended Claims 1 and 15 to recite "greater than 0.6 μm" and provides arguments supporting such amendments below.

The present application discloses methods for inducing polarized immune responses. Specifically, the application discloses the polarization of the T_H1 immune response over the T_H2 immune response and vice versa. The Examiner has presented a rejection under 35 U.S.C. §112, first paragraph, arguing that the specification fails to provide descriptive support for the method as now claimed in Claims 1 and 15. In particular, the Examiner asserts there is no basis for the lower size limit of 0.6 μm for the microparticles used in these methods.

Applicant respectfully traverses the Examiner's rejection. Applicant submits that the written description requirement is satisfied for the claimed numerical range (greater than 0.6 μm and less than 5 μm). The specification clearly supports claiming the use of microparticles with a lower size limit of greater than 600 nm (0.6 μm) to provide a T_H1 response.

The methods for inducing the different polarized immune responses require the administration of particles of different sizes. The immune response that is activated, T_H1 or T_H2, depends on the median size of the particles. This is summarized on page 5, line 13, to page 6, line 2, of the application, which states:

> Accordingly, the present invention provides a method of inducing a T_H1 polarised immune response to an antigen(s), comprising parenterally

administering to a subject, such as a mammal and preferably a human, microparticles sized such that at least 50% of the microparticles are less than 5 μm, preferably less than 3 μm, the microparticles comprising the antigen(s) entrapped or encapsulated by a biodegradable polymer. A vaccine formulation for parenteral administration comprising microparticles sized such that at least 50% of the microparticles are less than 5 μm, preferably less than 3 μm, the microparticles comprising the antigen(s) entrapped or encapsulated by a biodegradable polymer is also provided.

Additionally, the present invention provides a method of inducing a T_H2 polarised immune response to an antigen(s), comprising parenterally administering to a subject, such as a mammal and preferably a human, nanoparticles sized such that at least 50% of the nanoparticles are less than 600 nm, preferably less than 500 nm, the nanoparticles comprising the antigen(s) entrapped or encapsulated by a biodegradable polymer. A vaccine formulation for parenteral administration comprising nanoparticles sized such that at least 50% of the nanoparticles are less than 600 nm, preferably less than 500 nm, the nanoparticles comprising the antigen(s) entrapped or encapsulated by a biodegradable polymer is also provided.

Thus, it is clear that the present application discloses two distinct subsets of particles: microparticles and nanoparticles. Furthermore, the present application requires that microparticles and nanoparticles each elicit two different polarized immune responses: T_H1 and T_H2, respectively. Thus, use of microparticles implies a polarized T_H1 response while use of nanoparticles implies a polarized T_H2 response. By definition, it is not possible to simultaneously have a *polarized* T_H1 response and a *polarized* T_H2 response. As these two polarized immune responses are mutually exclusive, it follows from the above sections of the specification that microparticles and nanoparticles are mutually exclusive subsets of particles. Thus, a microparticle cannot be a nanoparticle and vice versa.

The particles of the application are defined not only by the different immune responses they induce, but also by their median sizes. The application teaches that administration of particles with a median size less than or equal to 600 nm (0.6 μm) would induce a T_H2 response, thus making such particles nanoparticles. Similarly, the

median size of the T_H1-inducing microparticles must be less than or equal to 5 μm. Because a polarizing T_H1-inducer cannot be a polarizing T_H2-inducer, a microparticle cannot be a nanoparticle. Because microparticles cannot be nanoparticles, the median sizes of these two particle types cannot be the same. Therefore, because nanoparticles have a median size less than or equal to 0.6 μm, microparticles must have a median size greater than 0.6 μm. Upon a careful reading of the specification, one of skill in the art could come to no other conclusion. The examiner has asserted in the actions dated May 2, 2003 and November 29, 2002 that because the lower size limitation for microparticles has not been stated explicitly, there is no support in the specification for this lower size limitation. This position fails to consider that the above cited sections of the specification clearly delineate upper and lower median sizes of the T_H1-induciong microparticles. The fact that the median size of the T_H1-inducing microparticles must be greater than 0.6 μm is an inherent characteristic of the T_H1-inducing microparticles, and need not be stated explicitly. MPEP §2163.07(a) states:

> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

In the present case, no extrinsic evidence is necessary to establish inherency. As discussed above, the present application indicates that there is no overlap between the median sizes of nanoparticles and microparticles. T_H2-inducing nanoparticles inherently have a median size less than or equal to 600 nm (0.6 μm). Thus, it is an inherent characteristic of T_H1-inducing microparticles that their median size is greater than 0.6 μm. Because this is an inherent characteristic of T_H1-inducing microparticles, applicant submits that the recitation "greater than 0.6 μm" is not new matter, rather, it is an inherent characteristic of T_H1-inducing microparticles and is supported by the

specification.

Applicant submits that given the teaching in the specification that particles with a median size greater than 600 nm (0.6 μm) induced a T_H1 response, applicant may combine the upper limit of 5 μm with the clearly delineated lower limit of 600 nm (0.6 μm). The Examiner is again directed to Claim 7 as originally filed, which made clear that 600 nm was the upper limit for a T_H2 response. In presenting the rejection of Claims 1 and 15, the Examiner has repeatedly pointed out that Claim 7 relates to non-elected subject matter. Applicant submits that whether or not this matter is elected is not relevant. "In establishing a disclosure, applicant may rely not only on the description and drawing as filed but also on the original claims if their content justifies it." MPEP §608.01(l). Thus, applicant can rely on the entire specification as filed to support claim amendments and does not "lose" the disclosure which relates to non-elected subject matter.

In addition, the terms "particle", "nanoparticle", and "microparticle" are all used in the present application and one of skill in the art would not be confused as to the meaning of these terms. As an example, the term "particle" is used generically to describe the particles greater than and less than 600 nm on page 19 of the application.

Finally, the manufacture and identification of particles greater than 0.6 μm is routine and is clearly enabled. The Examiner is respectfully directed to page 19, line 23, to page 20, line 1, of the present specification, which discusses particle size assessment by SEM. This section of the specification indicates that particles greater than 600 nm (0.6 μm) were made using the disclosed techniques and could be identified using SEM analysis.

In view of the preceding argument, applicant respectfully requests that the rejections under 35 U.S.C. §112, first paragraph, as containing new subject matter be

withdrawn.

Respectfully submitted,

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